

IN THE CLAIMS

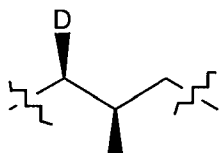
1. (Previously presented) An HIV protease inhibitor represented by a formula:

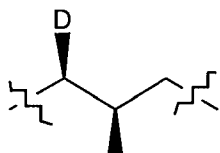


wherein

X is a 5-7 membered non-aromatic monocyclic heterocycle, wherein said heterocycle is fused or bridged with one or more 3-7 membered non-aromatic monocyclic heterocycle to form a polycyclic system, wherein any of said heterocyclic ring systems contains one or more heteroatoms selected from O, N, S, or P; wherein any nitrogen forming part of the heterocycles may optionally be substituted by R₂, R₃, R₆, R₇ or O; wherein any sulfur may be optionally be substituted by one or two oxygen atoms; wherein any P may be optionally be substituted by one or more of O NR₂, or S, and any of said ring systems optionally contains 1 to 6 substituents selected from the group consisting of R₂, R₃, R₅, and R₆;

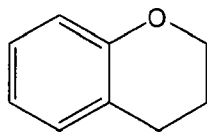
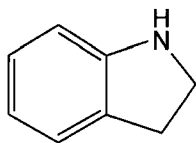
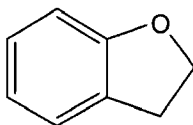
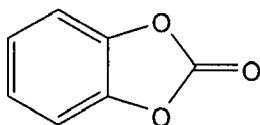
A is ZCZNH, wherein Z is;



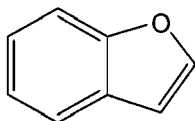
B is , wherein D is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, or aralkyl optionally substituted with one or more groups selected from alkyl, halo, nitro, cyano, CF₃, C₃-C₇ cycloalkyl, or C₅-C₇ cycloalkenyl;

A' is N(D')E', wherein D' is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, or aralkyl optionally substituted by alkyl, halo, nitro, cyano, CF₃, O-alkyl, or S-alkyl, and E' is -CO- or -SO₂-;

X' is selected from the group consisting of (a)



or



wherein said groups are substituted with one or more of the following groups:

OR3, OR6, OR7, OR2 provided R2 is not H or unsubstituted alkyl;

alkyl substituted by R3, R5, R6 provided R5 is not halo;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, and heterocyclo, which groups may be optionally substituted with one or more substituents selected from R5;

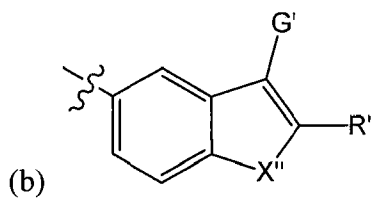
aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from the group consisting of aryl, heteroaryl, R2, R3, R4, and R6;

C3-C7 cycloalkyl substituted by R2, R3, R5, R6; provided R2 is not H;

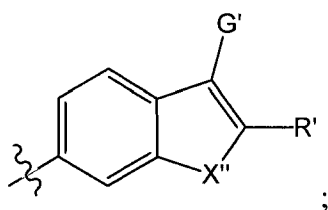
CO₂H or R7; provided R8 is not H or unsubstituted alkyl;

NR₈R₈, NR₇R₈, NR₇R₇; provided R8 is not H or unsubstituted alkyl; and

$\text{SO}_n\text{N}(\text{R}_8)_2$, $\text{SO}_n\text{NR}_7\text{R}_8$, SR_8 , $\text{S}(\text{O})_n\text{R}_8$, provided R_8 is not H or methyl;
 and n is 1 or 2,



or



wherein

G' and R' cannot both be H;

G' and R' are each independently:

H or alkyl substituted by R_3 , R_5 , R_6 provided R_5 is not halo;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, and heterocyclo, which groups may be optionally substituted with one or more substituents selected from the group consisting of $-\text{OR}_2$, $\text{C}(\text{O})\text{N}(\text{R}_2)_2$, $\text{S}(\text{O})_n\text{N}(\text{R}_2)_2$, CN, SR_2 , SO_nR_2 , COR_2 , CO_2R_2 or $\text{NR}_2\text{C}(\text{O})\text{R}_2$, R_5 , and R_7 ;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from the group consisting of aryl, heteroaryl, R_2 , R_3 , R_4 , and R_6 ;

C3-C7 cycloalkyl substituted by R_2 , R_3 , R_5 , R_6 ; provided R_2 is not H;

CO_2H or R_7 provided R_2 is not H or unsubstituted alkyl;

$\text{SO}_n\text{N}(\text{R}_8)_2$, $\text{SO}_n\text{NR}_7\text{R}_8$, SR_8 , $\text{S}(\text{O})_n\text{R}_8$, provided R_8 is not H or methyl; and n is 1 or 2;

and X'' is selected from O or NR'';

wherein R'' is

H or alkyl optionally substituted by R3, R5, R6;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl,
and heterocyclo, which groups may be optionally substituted with one or
more substituents selected from the group consisting of -OR2,
C(O)N(R2)₂, S(O)_nN(R2)₂, CN, SR2, SO_nR2, COR2, CO₂R2 or
NR2C(O)R2, R5, and R7;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally
substituted with one or more groups selected from the group consisting of
aryl, heteroaryl, R2, R3, R4, and R6;

C3-C7 cycloalkyl optionally substituted by R2, R3, R5, R6;

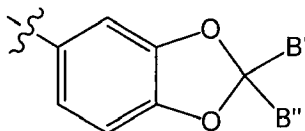
R7;

NR3R3, NR6R6, NR7R7, NR3R6, NR6R7, NR3R7, NR2R3, NR2R6,
NR2R7, NR2R2;

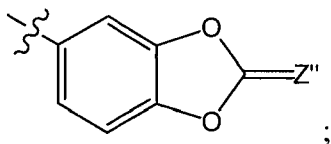
SO_nN(R2)₂, SO_nN(R3)₂, SO_nN(R6)₂, SO_nN(R7)₂, SO_nNR2R3,
SO_nNR2R6, SO_nNR2R7, SO_nNR3R6, SO_nNR3R7, SO_nNR6R7;

S(O)_mR2, S(O)_mR3, S(O)_mR6, provided R2 is not H; and m is 0, 1 or 2;

(c)



or



wherein

B' and B'' cannot both be H or methyl;

B' and B'' are independently:

H or alkyl optionally substituted by R3, R5, R6;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, and heterocyclo, which groups may be optionally substituted with one or more substituents selected from the group consisting of -OR2, C(O)N(R2)2, S(O)_nN(R2)2, CN, SR2, SO_nR2, COR2, CO₂R2 or NR2C(O)R2, R5, and R7;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from the group consisting of aryl, heteroaryl, R2, R3, R4, and R6;

C3-C7 cycloalkyl optionally substituted by R2, R3, R5, R6;

CO₂H or R7;

SO_nN(R2)2, SO_nN(R3)2, SO_nN(R6)2, SO_nN(R7)2, SO_nNR2R3, SO_nNR2R6, SO_nNR2R7, SO_nNR3R6, SO_nNR3R7, SO_nNR6R7;

S(O)_mR2, S(O)_mR3, S(O)_mR6; and m is 0, 1 or 2;

Z'' is O, NR9;

R9 is alkyl optionally substituted by R3, R5, R6;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, and heterocyclo, which groups may be optionally substituted with one or more

substituents selected from the group consisting of -OR₂, C(O)N(R₂)₂, S(O)_nN(R₂)₂, CN, SR₂, SO_nR₂, COR₂, CO₂R₂ or NR₂C(O)R₂, R₅, and R₇;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from the group consisting of aryl, heteroaryl, R₂, R₃, R₄, and R₆;

C3-C7 cycloalkyl optionally substituted by R₂, R₃, R₅, R₆;

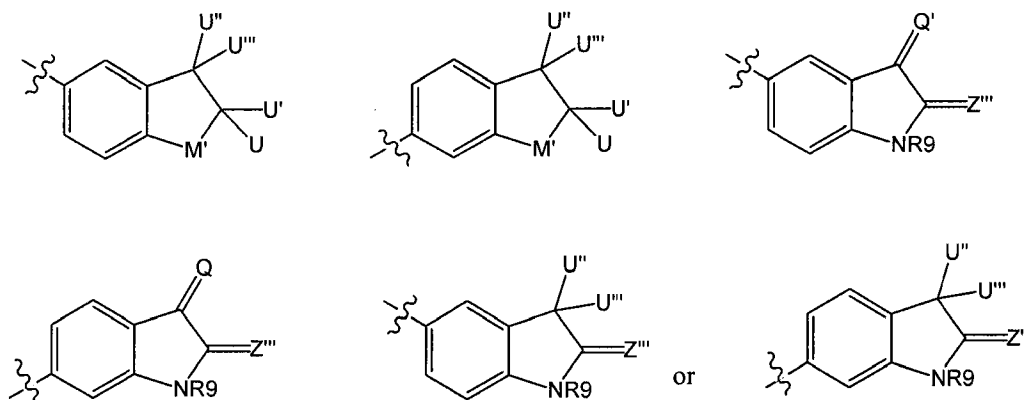
CO₂H or R₇;

NR₃R₃, NR₆R₆, NR₇R₇, NR₃R₆, NR₆R₇, NR₃R₇, NR₂R₃, NR₂R₆, NR₂R₇, NR₂R₂;

SO_nN(R₂)₂, SO_nN(R₃)₂, SO_nN(R₆)₂, SO_nN(R₇)₂, SO_nNR₂R₃, SO_nNR₂R₆, SO_nNR₂R₇, SO_nNR₃R₆, SO_nNR₃R₇, SO_nNR₆R₇;

S(O)_mR₂, S(O)_mR₃, S(O)_mR₆, provided R₂ is not H; and m is 0, 1 or 2, or

(d)



wherein

U and U' are each independently

H or alkyl substituted by R₃, R₅, R₆;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, and heterocyclo, which groups may be optionally substituted with one or more

substituents selected from the group consisting of -OR₂, C(O)N(R₂)₂, S(O)_nN(R₂)₂, CN, SR₂, SO_nR₂, COR₂, CO₂R₂ or NR₂C(O)R₂, R₅, and R₇;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from the group consisting of aryl, heteroaryl, R₂, R₃, R₄, and R₆;

C₃-C₇ cycloalkyl substituted by R₂, R₃, R₅, R₆;

CO₂H, R₇;

SO_nN(R₂)₂, SO_nN(R₃)₂, SO_nN(R₆)₂, SO_nN(R₇)₂, SO_nNR₂R₃, SO_nNR₂R₆, SO_nNR₂R₇, SO_nNR₃R₆, SO_nNR₃R₇, SO_nNR₆R₇, wherein n= 1 or 2;

S(O)_mR₂, S(O)_mR₃, S(O)_mR₆, provided R₂ is not H; and n is 0, 1 or 2;

U'' and U''' are each independently

H, OR₃, OR₆, OR₇, OR₂;

alkyl substituted by R₃, R₅, R₆;

C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₈ cycloalkyl, C₅-C₈ cycloalkenyl, and heterocyclo, which groups may be optionally substituted with one or more substituents selected from the group consisting of -OR₂, C(O)N(R₂)₂, S(O)_nN(R₂)₂, CN, SR₂, SO_nR₂, COR₂, CO₂R₂ or NR₂C(O)R₂, R₅, and R₇;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from the group consisting of aryl, heteroaryl, R₂, R₃, R₄, and R₆;

C₃-C₇ cycloalkyl substituted by R₂, R₃, R₅, R₆;

CO₂H or R₇;

NR3R3, NR6R6, NR7R7, NR3R6, NR6R7, NR3R7, NR2R3, NR2R6, NR2R7,
NR2R2;

SO_nN(R2)₂, SO_nN(R3)₂, SO_nN(R6)₂, SO_nN(R7)₂, SO_nNR2R3, SO_nNR2R6,
SO_nNR2R7, SO_nNR3R6, SO_nNR3R7, SO_nNR6R7;

S(O)_mR2, S(O)_mR3, S(O)_mR6, provided R2 is not H; and m is 0, 1 or 2;

U and U' cannot both be H unless one of U'' and U''' is not H;

U'' and U''' cannot both be H unless one of U and U' is not H;

M' is O, NR9, or NH, except where R9 is CO₂H

Z''' is O or NR9

Q' is O, NR9, or CU''U''';

R9 is

alkyl optionally substituted by R3, R5, R6;

C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, and
heterocyclo, which groups may be optionally substituted with one or more
substituents selected from the group consisting of -OR2, C(O)N(R2)₂,
S(O)_nN(R2)₂, CN, SR2, SO_nR2, COR2, CO₂R2 or NR2C(O)R2, R5, and R7;

aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted
with one or more groups selected from the group consisting of aryl, heteroaryl,
R2, R3, R4, and R6;

C3-C7 cycloalkyl optionally substituted by R2, R3, R5, R6;

CO₂H or R7;

NR3R3, NR6R6, NR7R7, NR3R6, NR6R7, NR3R7, NR2R3, NR2R6, NR2R7,
NR2R2;

SO_nN(R2)₂, SO_nN(R3)₂, SO_nN(R6)₂, SO_nN(R7)₂, SO_nNR2R3, SO_nNR2R6,
SO_nNR2R7, SO_nNR3R6, SO_nNR3R7, SO_nNR6R7;

S(O)_mR2, S(O)_mR3, S(O)_mR6, provided R2 is not H; and m is 0, 1 or 2

wherein R is H or alkyl, aryl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclo,
heteroaryl; optionally substituted by halo, hydroxy, alkoxy, aryloxy, cycloalkoxy,
heteroaryloxy, cyano, nitro, alkylthio, arylthio, cycloalkylthio, amino, or mono- or
dialkylamino, mono- or diarylamino, mono- or di-cycloalkylamino, mono- or di-
heteroarylamino, alkanoyl, cycloalkanoyl, aroyl, heteroaroyl, carboxamido, mono- or
dialkylcarboxamido, mono- or diarylcarboxamido, sulfonamido, mono- or
dialkylsulfonamido, mono- or diarylsulfonamido, alkylsulfinyl, alkylsulfonyl,
arylsulfinyl, arylsulfonyl, cycloalkylsulfinyl, cycloalkylsulfonyl, heteroarylsulfinyl,
heteroarylsulfonyl;

R2 is H or C1-C6 alkyl; optionally substituted by C2-C6 alkenyl, C2-C6 alkynyl, C3-
C8 cycloalkyl, C5-C8 cycloalkenyl, heterocyclo; which groups may be optionally
substituted with one or more substituents selected from the group consisting of halo, OR,
ROH, R-halo, NO₂, CN, CO_nR, CON(R)₂, C(S)R, C(S)N(R)₂, SO_nN(R)₂, SR, SO_nR,
N(R)₂, N(R)CO_nR, NRS(O)_nR, NRC[=N(R)]N(R)₂, N(R)N(R)CO_nR, NRPO_nN(R)₂,
NRPO_nOR, oxo, =N-OR, =N-N(R)₂, =NR, =NNRC(O)N(R)₂, =NNRCO_nR,
=NNRS(O)_nN(R)₂, or =NNRS(O)_n(R);

or R2 is C1-C6 alkyl; substituted by aryl or heteroaryl; which groups may be
optionally substituted with one or more substituents selected from the group
consisting of halo, OR, ROH, R-halo, NO₂, CN, CO_nR, CON(R)₂, C(S)R,
C(S)N(R)₂, SO_nN(R)₂, SR, SO_nR, N(R)₂, N(R)CO_nR, NRS(O)_nR,
NRC[=N(R)]N(R)₂, N(R)N(R)CO_nR, NRPO_nN(R)₂, NRPO_nOR;

or R2 is C1-C6 alkyl; optionally substituted by halo, OR, ROH, R-halo, NO₂, CN, CO_nR, CON(R)₂, C(S)R, C(S)N(R)₂, SO_nN(R)₂, SR, SO_nR, N(R)₂, N(R)CO_nR, NRS(O)_nR, NRC[=N(R)]N(R)₂, N(R)N(R)CO_nR, NRPO_nN(R)₂, NRPO_nOR, oxo, =N-OR, =N-N(R)₂, =NR, =NNRC(O)N(R)₂, =NNRCONR, =NNRS(O)_nN(R)₂, or =NNRS(O)_n(R);

R3 is C2-C6 alkenyl, C2-C6 alkynyl, C3-C8 cycloalkyl, C5-C8 cycloalkenyl, or heterocyclo; which groups may be optionally substituted with one or more substituents selected from the group consisting of halo, OR₂, R₂-OH, R₂-halo, NO₂, CN, CO_nR₂, C(O)N(R₂)₂, C(O)N(R₂)N(R₂)₂, C(S)R₂, C(S)N(R₂)₂, S(O)_nN(R₂)₂, SR₂, SO_nR₂, N(R)₂, N(R₂)CO_nR₂, NR₂S(O)_nR₂, NR₂C[=N(R₂)]N(R₂)₂, N(R₂)N(R₂)CO_nR₂, NR₂PO_nN(R₂)₂, NR₂PO_nOR₂, oxo, =N-OR₂, =N-N(R₂)₂, =NR₂, =NNRC(O)N(R₂)₂, =NNR₂C(O)_nR₂, =NNR₂S(O)_nN(R₂)₂, or =NNR₂S(O)_n(R₂);

R4 is halo, OR₈, R₂-OH, R₃-OH, R₂-halo, R₃-halo, NO₂, CN, CO_nR₈, CO_nR₈, CON(R₈)₂, C(O)N(R₈)N(R₈)₂, C(S)R₈, C(S)N(R₈)₂, SO_nN(R₈)₂, SR₈, SO_nR₈, N(R₈)₂, N(R₈)CO_nR₈, NR₈S(O)_nR₈, NR₈C[=N(R₈)]N(R₈)₂, N(R₈)N(R₈)CO_nR₈, NR₈PO_nN(R₈)₂, NR₈PO_nOR₈, OC(O)R₂, OC(S)R₈, OC(O)N(R₈)₂, OC(S)N(R₈)₂, OPO_n(R₈)₂;

R5 is OR₈, N(R₈)₂, NHOH, N(R₈)COR₈, NR₈S(O)_nR₈, NR₈C[=N(R₈)]N(R₈)₂, N(R₈)N(R₈)C(O)R₈, NR₈PO_nN(R₈)₂, NR₈PO_nOR₈, R₂OH, R₃-OH, R₂-halo, R₃-halo, CN, CO_nR₈; provided that when n = 2, R₈ is not H; CON(R₈)₂, C(O)N(R₈)N(R₈)₂, C(S)_nR₈, C(S)N(R₈)₂, S(O)_nR₈, SO_nN(R₈)₂, halo, NO₂, SR₈, oxo, =N-OH, =N-OR₈, =N-N(R₈)₂, =NR₈, =NNR₈C(O)N(R₈)₂, =NNR₈C(O)_nR₈, =NNR₈S(O)_nN(R₈)₂, or =NNR₈S(O)_n(R₈), or R3

R6 is aryl or heteroaryl, wherein said aryl or heteroaryl may be optionally substituted with one or more groups selected from aryl, heteroaryl, R₂, R₃, halo, OR₂, R₂OH, R₂-halo, NO₂, CN, CO_nR₂, C(O)N(R₂)₂, C(O)N(R₂)N(R₂)₂, C(S)R₂, C(S)N(R₂)₂, S(O)_nN(R₂)₂, SR₂, SO_nR₂, N(R)₂, N(R₂)CO_nR₂, NR₂S(O)_nR₂, NR₂C[=N(R₂)]N(R₂)₂,

$N(R_2)N(R_2)CO_nR_2$, $NR_2PO_nN(R_2)_2$, $NR_2PO_nOR_2$, $OC(O)R_2$, $OC(S)R_2$, $OC(O)N(R_2)_2$,
 $OC(S)N(R_2)_2$, $OPO_n(R_2)_2$.

R_7 is $C(O)_nR_8$; provided that when $n = 2$; R_8 is not H; $C(S)R_8$, $C(O)N(R_8)_2$,
 $C(S)N(R_8)_2$, $S(O)_nR_8$, $S(O)_nN(R_8)_2$;

R_8 is R_2 , R_3 , or R_6 ;

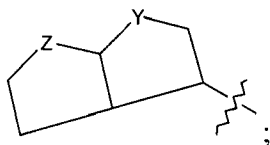
each n is independently 1 or 2;

its stereoisomeric forms; and

its pharmacologically acceptable salts.

2. (Currently amended) The **HIV protease inhibitor** compound according to claim 1,
 wherein

X is



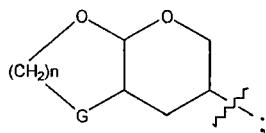
Y is O, NH, or S;

Z is O, NH, or S; and

wherein any ring carbon is optionally substituted by R_2 , R_3 , R_5 , or R_6 ..

3. (Currently amended) The **HIV protease inhibitor** compound according to claim 1,
 wherein

X is



wherein

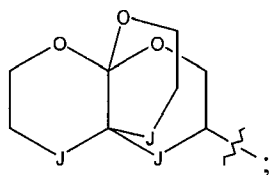
G is C, O, NR₂, or S;

n is an integer between 1-2; and

wherein any ring carbon is optionally substituted by R₂, R₃, R₅, or R₆.

4. (Currently amended) The **HIV protease inhibitor** compound according to claim 1, wherein

X is



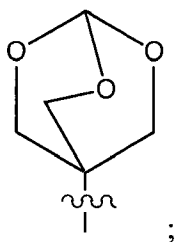
wherein

J is independently CH₂, or O, and

wherein any ring carbon is optionally substituted by R₂, R₃, R₅, or R₆.

5. (Currently amended) The **HIV protease inhibitor** compound according to claim 1, wherein:

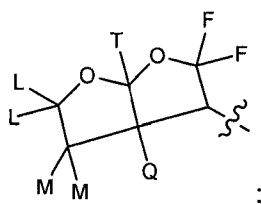
X is



wherein any ring carbon is optionally substituted by R2, R3, R5, or R6.

6. (Currently amended) The **HIV protease inhibitor** compound according to claim 1, wherein

X is



wherein

each L is independently H, lower alkyl, oxo, or L forms a carbocyclic or heterocyclic ring with M;

each M is independently H, OH, chloro, fluoro, or M forms a carbocyclic or heterocyclic ring with Q, provided that if one M is OH, the other M is not OH;

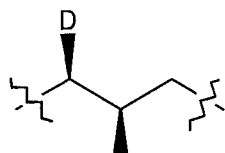
Q is H, OH, amino, lower alkyl, alkylamino, alkoxy, halo, or forms a 3-7-membered carbocyclic or heterocyclic ring together with T;


each F is independently H, OH, lower alkyl, halo, or spirocyclopropyl, provided that if one R is OH, the other R is not OH;

T is H or F, or T forms a carbocyclic or heterocyclic ring together with F.

7. (Previously presented) The HIV protease inhibitor according to claim 1, wherein

X is tetrahydrofurodihydrofuranyl, tetrahydrofurotetrahydrofuranyl, tetrahydropyranotetrahydrofuranyl or tetrahydropyranodihydrofuranyl;

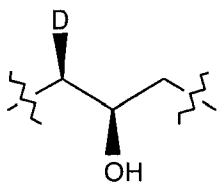



B is , wherein D is selected from alkyl, alkenyl, alkynyl, aryl, cycloalkyl, or aralkyl optionally substituted with one or more groups selected from alkyl, halo, nitro, cyano, CF₃, C3-C7 cycloalkyl, C5-C7 cycloalkenyl, R₆, OR₂, SR₂, NHR₂, OR₃, SR₃, NHR₃, OR₆, SR₆, or NHR₆; and

A' is N(D')E', wherein D' is alkyl, alkenyl, alkynyl aryl, cycloalkyl, or aralkyl optionally substituted by alkyl, halo, or CF₃, and E' is -SO₂-.

8. (Previously presented) The HIV protease inhibitor according to claim 1, wherein:

X is tetrahydrofurotetrahydrofuranyl;

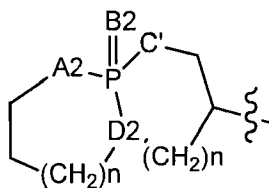


B is , wherein D is benzyl; and

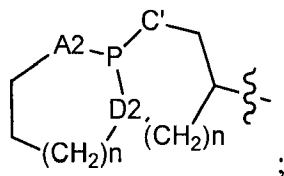
A' is N(D')E', wherein D' is isobutyl and E' is -SO₂-;

9. (original) The HIV protease inhibitor according to claim 1, wherein

X is



or



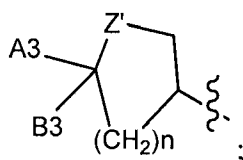
wherein A2, B2, and C' are each independently O, NR₂, or S;

D2 is CH or N; and

n is an integer between 1 and 2.

10. (original) The HIV protease inhibitor according to claim 1, wherein:

X is



wherein

A3 is H, F or alkoxy;

B3 is F, alkoxy, lower alkyl, or A3 and B3 can form a 3-7 membered heterocyclic ring;

Z' is O, NR₂, or S; and

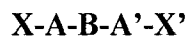
n is an integer between 1-3.

11-15. (Canceled)

16. (Currently amended) A The HIV protease inhibitor compound according to claim 1, bound in a complex with wild type or drug resistant mutant forms of HIV-1 protease.

17. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 1 and a pharmaceutically acceptable additive, excipient, or diluent.

18. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 1 and ~~another~~ an antiretroviral agent.
19. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 1 and a second HIV inhibitor.
20. (Currently amended) A pharmaceutical composition comprising an HIV protease inhibitor according to claim 1 and ~~an additional~~ a second HIV protease inhibitor.
21. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 1 and an HIV reverse transcriptase inhibitor.
22. (Currently amended) A method of treating a patient suffering from HIV infection, comprising administering to said patient a composition according to claim 1 ~~+~~ 17.
23. (original) A method of treatment according to claim 22 wherein said patient is suffering from a multi-drug resistant HIV infection.
24. (Currently amended) An HIV protease inhibitor according to claim 1 having the formula I:



I

wherein X is a moiety comprising first and second hydrogen bond acceptor atoms $H_{A1}:X$ and $H_{A2}:X$, wherein $H_{A1}:X$ forms a hydrogen bond with N29 of HIV protease and $H_{A2}:X$ forms a hydrogen bond with N30 of HIV protease at the relative positions designated in Table 8;

wherein A is an optionally substituted linker moiety comprising a linear chain of 2-6 atoms, wherein A comprises a hydrogen bond acceptor atom $H_A:A$, and a hydrogen bond

donor atom $H_D:A$, and wherein $H_A:A$ forms a hydrogen bond with solvated water³⁰¹ of said protease at a relative position designated by O301, and $H_D:A$ forms a hydrogen bond with the backbone CO atom of residue 27 of said protease at a relative position designated by O27;

wherein B comprises a hydrogen bond donor or acceptor atom $H_{D/A}:B$, wherein $H_{D/A}:B$ forms a hydrogen bond with either or both carboxylate side chain oxygens of Asp25 and Asp 125 of said protease at relative positions designated by OD1 25, OD2 25, OD1 125, and OD2 125;

wherein A' is an optionally substituted linker moiety comprising a linear chain of 2-6 atoms, comprising a hydrogen bond acceptor atom $H_A:A'$, wherein $H_A:A'$ forms a hydrogen bond with solvated water³⁰¹ of said protease at a relative position designated by O301; and

wherein X' is a moiety comprising a hydrogen bond acceptor atom $H_A:X'$, wherein $H_A:X'$ forms a hydrogen bond with backbone NH atoms of residues 129 and/or 130 of said protease at relative positions designated by N129 and/or N130.

25. (Currently amended) An HIV protease inhibitor ~~A compound~~ according to claim 24, bound in a complex with wild type or drug resistant mutant forms of HIV-1 protease.
26. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 24 and a pharmaceutically acceptable additive, excipient, or diluent.
27. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 24 and ~~another~~ an antiretroviral agent.
28. (Currently amended) A pharmaceutical composition comprising an effective amount of an HIV protease inhibitor according to claim 24 and a second HIV inhibitor.
29. (Currently amended) A pharmaceutical composition comprising an HIV protease inhibitor according to claim 24 and ~~an additional~~ a second HIV protease inhibitor.

30. (Currently amended) A pharmaceutical composition comprising an effective amount of an **HIV protease** inhibitor according to claim 24 and an HIV reverse transcriptase inhibitor.

31. (Currently amended) A method of treating a patient suffering from HIV infection, comprising administering to said patient a composition according to claim 24 **26**.

32. (original) A method of treatment according to claim 31 wherein said patient is suffering from a multi-drug resistant HIV infection.